AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for reducing amyloid plaque burden in a mammal comprising effecting presentation to said mammal's immune system of an immunogenically effective amount of an analogue of said mammal's autologous Aβ or autologous APP wherein is introduced at least one ~~isolated~~ foreign T helper epitope by means of insertion of an amino acid sequence into said autologous Aβ or autologous APP or substitution of at least one amino acid sequence within the autologous Aβ or APP with an amino acid sequence of equal or different length, ~~addition, deletion, or substitution~~, wherein said foreign T helper epitope is selected from a group consisting of Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, a *P.falciparum* CS epitope and an artificial MHC-II binding peptide sequence; whereby immunization of said mammal with said analogue induces production of antibodies against the autologous Aβ or autologous APP in said mammal.

2. (Cancelled)

3. (Previously Presented) The method according to claim 1, wherein the introduction further comprises:

- at least one first moiety which is a specific binding partner, selected from the group consisting of a hapten and a carbohydrate, for a B-lymphocyte specific surface antigen or an antigen presenting cell (APC) specific surface antigen, which targets the analogue to an antigen presenting cell (APC) or a B-lymphocyte,

- at least one second moiety selected from the group consisting of a cytokine, heat shock protein or hormone, which, stimulates the immune system, and/or

- at least one third moiety selected from the group consisting of a lipid and a polyhydroxypolymer, which optimizes presentation of the analogue to the immune system.

4. (Previously Presented) The method according to claim 3, wherein the analogue is modified by introducing side groups, by covalent or non-covalent binding to suitable chemical groups in Aβ or APP, or a subsequence thereof, of the first and/or of the second and/or of the third moiety.

5. (Cancelled)

6. (Cancelled)

7. (Currently Amended) The method according to claim 1, wherein introduction of said at least one T helper epitope is by insertion of at least one isolated T helper epitope in said autologous Aβ or autologous APP and~~the amino acid substitution, deletion, insertion and/or addition~~ results in a substantial preservation of the overall tertiary structure of Aβ or APP.

8. (Previously Presented) The method according to claim 1, wherein the analogue includes a duplication of at least one B-cell epitope of the amyloidogenic polypeptide and/or an introduction of a hapten.

9. (Currently Amended) The method according to claim 1, wherein the foreign T-cell epitope is immunodominant in the mammal.

10. (Previously Presented) The method according to claim 1, wherein the foreign T-cell epitope is promiscuous.

11. (Cancelled)

12. (Cancelled) The method according to claim 3, wherein the first moiety is selected from a substantially specific binding partner for a B-lymphocyte specific surface antigen and a substantially specific binding partner for an APC specific surface antigen.

13. (Cancelled) The method according to claim 3, wherein the second moiety is selected from a cytokine, a hormone, and a heat-shock protein.

14 - 16. (Cancelled)

17. (Previously Presented) The method according to claim 1, wherein the autologous Aβ or APP has been modified so as to preserve B-cell epitopes which are not exposed to the extracellular phase when present in a cell-bound form of the autologous APP.

18. (Previously Presented) The method according to claim 17, wherein the autologous Aβ or APP has been modified so as to lack at least one B-cell epitope which is exposed to the extracellular phase when present in a cell-bound form of the autologous APP.

19. (Currently Amended) The method according to claim 1 ~~which~~wherein introduction of said foreign T helper epitope comprises a substitution of at least one amino acid sequence within the autologous Aβ or APP with an amino acid sequence of equal or different length which gives rise to a foreign T_H epitope in the analogue.

20. (Cancelled)

21. (Cancelled)

22. (Cancelled)

23. (Cancelled)

24. (Cancelled)

25. (Previously Presented) The method according to claim 1, wherein presentation to the immune system is effected by having at least two copies of the analogue covalently or non-covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants.

26. (Previously Presented) The method according to claim 1, wherein the analogue has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

27 –29 (Cancelled)

30-32 (Cancelled)

33. (Previously Presented) The method according to claim 1, which includes at least one administration per year.

34-58 (Cancelled)

59. (Previously Presented) The method according to claim 10, wherein the foreign T-cell epitope is selected from a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence.

60. (Previously Presented) The method according to claim 1, wherein the tetanus toxoid epitope is selected from the group consisting of SEQ ID NO: 4 and SEQ ID NO: 6.

61. (Cancelled)

62. (Previously Presented) The method according to claim 3, wherein the cytokine is selected from the group consisting of interferon γ, Flt3L, interleukin 1, interleukin 2, interleukin 4, interleukin 6, interleukin 12, interleukin 13, interleukin 15, and granulocyte-macrophage colony stimulating factor.

63. (Previously Presented) The method according to claim 3, wherein the heat shock protein is selected from the group consisting of HSP70, HSP90, HSC70, GRP94, and calreticulin.

64. (Previously Presented) The method according to claim 3, wherein the third moiety is a lipid selected from the group consisting of a palmitoyl group, a myristyl group, a farnesyl group, a geranyl-geranyl group, a GPI-anchor, and an N-acyl diglyceride group.

65. (Previously Presented) The method according to claim 3, wherein the polyhydroxypolymer is a polysaccharide.

66. (Previously Presented) The method according to claim 33, comprising at least 2 administrations per year.

67. (Previously Presented) The method according to claim 66, comprising at least 3 administrations per year.

68. (Previously Presented) The method according to claim 27, wherein the parenteral route is selected from the group consisting of the subcutaneous, the intracutaneous, and the intramuscular route.

69. (Previously Presented) The method according to claim 1, wherein the artificial MHC-II binding peptide sequence is the amino acid sequence of SEQ ID NO. 19.

70. (Cancelled)

71. (Currently Amended) A method for reducing amyloid plaque burden in a mammal, the method comprising:

-administering an immunogenically effective amount of at least one modified Aβ or APP polypeptide, wherein said modified Aβ or APP polypeptide differs from the mammal's autologous Aβ or autologous APP polypeptide in that it comprises at least one isolated foreign T helper epitope <u>inserted into said autologous Aβ or autologous APP polypeptide and wherein said at least one isolated T helper epitope is</u> selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, a *P.falciparum* CS epitope and an artificial MHC-II binding peptide sequence

whereby administration to said mammal with said modified Aβ or APP polypeptide induces production of antibodies against the autologous Aβ or autologous APP polypeptide in said mammal.

72. (Previously Presented) The method according to claim 71, wherein said modified Aβ or APP polypeptide further comprises:

- at least one first moiety which is a specific binding partner, selected from the group consisting of a hapten and a carbohydrate, for a receptor on a B-lymphocyte or an antigen presenting cell (APC), which targets the modified Aβ or APP polypeptide to an antigen presenting cell (APC) or a B-lymphocyte, and/or

- at least one second moiety selected from the group consisting of a cytokine, heat shock protein or hormone, which stimulates the immune system, and/or

- at least one third moiety selected from the group consisting of a lipid and a polyhydroxypolymer, which optimizes presentation of the modified Aβ or APP polypeptide to the immune system.

73. (Cancelled)

74. (Currently Amended) A method for reducing amyloid plaque burden in a mammal, the method comprising:

-administering an immunogenically effective amount of at least one modified Aβ or APP polypeptide, wherein said modified Aβ or APP polypeptide differs from the mammal's autologous Aβ or autologous APP polypeptide in that it comprises at least one isolated foreign T helper epitope <u>inserted into said autologous Aβ or autologous APP polypeptide and wherein said at least one isolated T helper epitope is</u> selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, a *P.falciparum* CS epitope and a pan DR epitope peptide

whereby administration to said mammal with said modified Aβ or APP polypeptide induces production of antibodies against the autologous Aβ or autologous APP polypeptide in said mammal.

75. (Previously Presented) The method according to claim 74, wherein the modification further comprises:

- at least one first moiety which is a specific binding partner, selected from the group consisting of a hapten and a carbohydrate, for a receptor on a B-lymphocyte or an antigen presenting cell (APC), which targets the modified Aβ or APP polypeptide to an antigen presenting cell (APC) or a B-lymphocyte, and/or

- at least one second moiety selected from the group consisting of a cytokine, heat shock protein or hormone, which stimulates the immune system, and/or

- at least one third moiety selected from the group consisting of a lipid and a polyhydroxypolymer, which optimizes presentation of the modified Aβ or APP polypeptide to the immune system.

76. (Currently Amended) A method for reducing amyloid plaque burden in a mammal comprising effecting presentation to said mammal's immune system of an immunogenically effective amount of an analogue of said mammal's autologous Aβ or autologous APP wherein is introduced at least one ~~isolated~~ foreign T helper epitope by means of insertion of an amino acid sequence into said autologous Aβ or autologous APP or substitution of at least one amino acid sequence within the autologous Aβ or APP with an amino acid sequence of equal or different length, ~~addition, deletion, or substitution,~~ wherein said foreign T helper epitope is selected from a group consisting of Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, a *P.falciparum* CS epitope and a pan DR epitope peptide; whereby immunization of said mammal with said analogue induces production of antibodies against the autologous Aβ or autologous APP in said mammal.

77. (Previously Presented) A method according to claim 1, wherein the analogue is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,
- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714 of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;
- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;
- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and
- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672; and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.

78. (Previously Presented) A method according to 71, wherein the modified Aβ or APP polypeptide is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,
- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714

of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;

- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;
- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and
- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672; and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.

79. (Previously Presented) A method according to 74, wherein the modified Aβ or APP polypeptide is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,
- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714 of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;
- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;
- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,

- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and
- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672; and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.

80. (Previously Presented) A method according to 76, wherein the modified Aβ or APP polypeptide is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,
- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714 of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;
- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;
- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and

- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672; and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.

81. (New) The method according to claim 77, wherein the modified Aβ or APP polypeptide, from the N- to the C-terminus, consists of amino acid residues 672-714 of SEQ ID NO: 2 followed by SEQ ID NO: 4 followed by amino acid residues 672-714 of SEQ ID NO: 2 followed by SEQ ID NO: 6 followed by amino acid residues 672-714 of SEQ ID NO: 2.

82. (New) The method according to claim 77, wherein the modified Aβ or APP polypeptide, from the N- to the C-terminus, consists of amino acid residues 630-634 of SEQ ID NO: 2 followed by SEQ ID NO: 6 followed by SEQ ID NO: 4 followed by amino acid residues 671-714 of SEQ ID NO: 2.

83. (New) A method according to claim 77, wherein the modified Aβ or APP polypeptide, from the N- to the C-terminus, consists of amino acid residues 672-713 of SEQ ID NO: 2 followed by SEQ ID NO: 6 followed by amino acid residues 729-734 of SEQ ID NO: 2 followed by SEQ ID NO: 4 followed by amino acid residues 750-770 of SEQ ID NO: 2.